# ABSTRACTS

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**Comparison of two fluid-management strategies in acute lung injury**

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network; Wiedemann HP, Wheeler AP, Bernard GR, et al. N Engl J Med 2006;354:2564-75

**Conclusion:** A conservative strategy of fluid management in patients with acute lung injury shortens duration of mechanical ventilation without increasing nonpulmonary organ failure.

**Summary:** There is debate about optimal fluid management of patients with acute lung injury. Limiting fluids or inducing diuresis may improve lung function but at the expense of impaired perfusion of other organs. In this randomized study, a conservative or liberal strategy of fluid management in patients with acute lung injuries was used. The protocol was applied for 7 days in 1000 patients with acute lung injury. The primary end point was death at 60 days. Ventilator-free days and organ-failure-free days and measures of lung physiology were secondary end points. There was no difference between the two groups in the primary end point at 60 days. In the conservative strategy group, 25.5% of the patients died, and 28.4% of the patients died in the liberal strategy group ($P < .30$; 95% confidence interval for a difference, −2.6% to 8.4%). The cumulative fluid balance in the first 7 days in the conservative strategy group was −136 ± 491 mL. The cumulative fluid balance in the first 7 days in the liberal strategy group was +6992 ± 502 mL ($P < .001$). The conservative strategy group had an improved oxygenation index, lung injury score, and an increased number of ventilator-free days (14.6 ± 0.5 vs 12.1 ± 0.5, $P < .001$) vs the liberal strategy group. The conservative strategy group also had more days not spent in the intensive care unit (13.4 ± 0.4 vs 11.2 ± 0.4, $P < .001$) during the first 28 days. There was no difference between the conservative and liberal strategy groups with respect to prevalence of shock during the course of the study or the use of dialysis during the first 60 days (10% vs 14%, $P < .06$).

**Comment:** A conservative fluid management strategy did not decrease death at 60 days vs a liberal fluid management strategy in patients with acute respiratory distress syndrome. However, intensive care unit days were reduced and lung function was improved with the conservative fluid management posture. The results are consistent with other recent reports suggesting improved overall patient outcome with conservative fluid management in acute respiratory distress syndrome. The days of essentially drowning patients with acute lung injury to preserve distal organ perfusion should be over.

***Chlamydia pneumoniae* in foci of "early" calcification of the tunica media in atherosclerotic arteries; an incidental presence?**

Vobryshev YV, Lord RSA, Tran D. Am J Physio Heart Circ Physio 2006; 290:H1510-H1519

**Conclusion:** *Chlamydia pneumoniae* infection of medial smooth muscle cells may be crucial to calcification of the tunica media in atherosclerotic arteries.

**Summary:** The role of *C pneumoniae* infection in the pathogenesis of atherosclerosis continues to be debated. This study investigated a possible association between *C pneumoniae* infection and medial calcification. The authors obtained carotid endarterectomy specimens from 60 patients. The plaques were examined by polymerase chain reaction (PCR) and immunohistochemistry to identify presence of *C pneumoniae*. In this study, specimens that were double-positive (positive by both PCR and immunohistochemistry) were considered positive for the presence of *C pneumoniae*. Double-negative and single-positive results were analyzed separately. There were 17 specimens that were double-positive for *C Pneumoniae*. Twenty-two specimens were negative with respect to both PCR and immunohistochemistry, and 21 specimens showed single-positive results, being positive with either PCR or immunohistochemistry for *C pneumonia*, but not with both. Medial calcification was present in 58.8% (10 of 17) specimens double-positive for *C pneumoniae*. There was no medial calcification observed in any of the 22 specimens double-negative for *C pneumoniae*. In areas of medial calcification, electron microscopy indicated the presence of *C pneumoniae* in smooth muscle cells. These smooth muscle cells showed damage to the cytoplasm and basement membrane associated with elementary reticulate and aberrant bodies of *C pneumoniae*. Immunohistocytochemistry techniques confirmed the presence of *C pneumoniae* in smooth muscle cells.

**Comment:** There are two distinct forms of vascular calcification: intimal calcification, which occurs in the context of atherosclerosis, and medial calcification, which can occur without atherosclerosis. A variety of different mechanisms can contribute to vascular calcification. The present study suggests that the medial form of vascular calcification may be initiated by the infection of medial smooth muscle cells by *C pneumoniae*. Whether *C pneumoniae* is required for eventual narrowing of the arterial lumen or degeneration of the arterial wall is still unknown.

**Post high-intensity focused ultrasound enhances thrombolysis in an *in vitro* model**

Frenkel V, Oberoi J, Stone MJ, et al.Radiology 2006; 239:86-93

**Conclusion:** Thrombolysis with tissue plasminogen activator (tPA) can be enhanced using high-intensity pulsed focused ultrasound exposure.

**Summary:** Recent work has suggested ultrasound can serve as a adjunct to thrombolytic drugs with enhancement of thrombolysis (N Engl J Med 2004;351:2170-8). In the study summarized here, the authors sought to evaluate, in an in vitro model, the potential utility of pulsed high-intensity focused ultrasound to improve thrombolysis by tPA. Clots were created by placing 1 mL of human blood in isolated sections of Penrose tubes. There were four experimental groups: a control group of untreated clots, clots treated with tPA only, clots treated with only pulsed high-intensity ultrasound, and finally, a group treated with both tPA and pulsed high-intensity focused ultrasound. The efficacy of thrombolysis was measured by reduction in the mass of clot and by D-dimer levels. Experiments also were performed to evaluate dose-response curves for two ultrasound exposure parameters: number of pulses per raster point and total acoustic power. Compared with control clots, clots treated with focused ultrasound alone did not have increased levels of thrombolysis. Clots treated with focused ultrasound plus tPA had a 50% increase in degree of thrombolysis compared with clots treated with tPA only ($P < .001$). D-dimer assay results correlated with calculated degrees of thrombolysis. Clots treated with focused ultrasound plus tPA had a 53% higher release of D-dimer concentrations compared with clots treated with tPA only ($P < .001$). Increasing the number of pulses per raster point and total acoustic power resulted in corresponding increases in thrombolysis rates.

**Comment:** The use of a combination of thrombolytic drugs and focused ultrasound exposure has potential benefits, with possible quicker resolution of thrombus and lower doses of thrombolytic agents. These are changes that could result in decreased bleeding risk and decreased treatment times. Presumably ultrasound enhances thrombolysis through mechanical cavitation effects. A great deal of work will be required to evaluate the effective doses of both the ultrasound and thrombolytic agents in various clinical situations (eg, venous thrombi, arterial thrombi). Work such as this presented here establishes the feasibility of dose-ranging studies for thrombolytic agents and ultrasound for dissolving clots. Such work is crucial to future in vivo evaluation of a combination of ultrasound and thrombolytic agents.

**Correlates and long-term outcomes of angiographically proven stent thrombosis with sirolimus-paclitaxel-eluting stents**

Kuchulakanti PK, Chu WW, Torguson R. Circulation 2006;113:1108-13.

**Conclusion:** Renal failure, treatment of bifurcation lesions, in-stent restenosis, and cessation of clopidogrel therapy correlate with thrombosis of coronary artery stents.

**Summary:** Stent thrombosis is an infrequent, but serious complication of drug-eluting coronary artery stents. The authors sought to establish risk factors for coronary artery stent thrombosis associated with drug-eluting stents. A total of 2974 consecutive patients were treated with drug-eluting coronary artery stents, and 38 (1.27%) were identified by angiography to have evidence of stent thrombosis. Thrombosis of the stent occurred acutely in five patients, ≤30 days in 25 patients, and >30 days in eight patients. The authors compared procedural angiographic and clinical factors of the patients with stent thrombosis vs 2936 consecutive patients who were treated with drug-eluting stents for coronary disease and who did not experience stent thrombosis during a period of 12 months of follow-up. Patients with stent thrombosis compared with patients without stent thrombosis had a higher frequency of diabetes, postprocedural renal failure, and chronic renal failure. Patients with stent thrombosis had more bifurcation lesions and a trend toward smaller diameter stents. The incidence of discontinuation of clopidogrel therapy was higher in patients with stent thrombosis (36.8%) vs patients without stent thrombosis (10.7%, $P < .0001$). At 6 months, mortality was significantly higher in patients with stent thrombosis compared with those without stent thrombosis (31% vs 3%; $P < 0.001$). Multivariant analysis suggested renal failure, bifurcation lesions, in-stent restenosis, and cessation of clopidogrel therapy correlated with stent thrombosis ($P < .05$).